AMENDMENTS TO THE CLAIMS

Applicant has submitted a new complete claim set indicating marked up claims with insertions indicated by underlining and deletions indicated by strikeouts or double bracketing.

1. (Currently amended) A polypeptide or polypeptide construct comprising:
at least one single domain antibody directed against ~~any of~~ von Willebrand Factor (vWF).

2. (Previously presented) A polypeptide or polypeptide construct according to claim 1, comprising two or more single domain antibodies directed against vWF.

3.-21. (Canceled)

22. (Previously presented) A composition comprising a polypeptide or polypeptide construct according to claim 1 and a pharmaceutically acceptable vehicle.

23.-33. (Canceled)

34. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which the at least one single domain antibody directed against vWF is directed against vWF A1 domain, the A1 domain of activated vWF or the vWF A3 domain.

35. (Previously presented) A polypeptide or polypeptide construct according to claim 1 comprising two or more single domain antibodies, in which at least one single domain antibody is directed against vWF A1 domain, the A1 domain of activated vWF or the vWF A3 domain.

36. (Currently amended) A polypeptide or polypeptide construct according to claim 1, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

37. (Currently amended) A polypeptide or polypeptide construct according to claim 1, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation at high shear ($1600\ s^{-1}$) at 1 μg/ml or at lower concentrations; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

38. (Currently amended) A polypeptide or polypeptide construct according to claim 1, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65, or to:

an homologous sequence of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is a) able to inhibit at least 50% of platelet aggregation under high shear ($1600\ s^{-1}$) condition at 1 μg/ml or at lower concentrations, and b) not able to inhibit 50% of platelet aggregation under low shear ($300\ s^{-1}$) condition at 10 μg/ml or at lower concentrations; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that maintains the interaction with the target with affinity of 1×10^{-6} M or better; or

~~a functional~~ an antigen binding portion of any of SEQ ID NOs: 1 to 7, 23 to 31, and 62 to 65 that comprises a partial deletion of the complete amino acid sequence and still maintains the binding site(s) and protein domain(s) necessary for the binding of and interaction with the target.

39. (Withdrawn and currently amended) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand ~~Wilebrand~~ Factor, wherein the at least one single domain antibody corresponds to a sequence represented by any of SEQ ID NO: 3, or to an homologous sequence of SEQ ID NO: 3 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear ($1600\ s^{-1}$) condition at 1 μg/ml or at lower concentrations.

40. (Currently amended) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand ~~Wilebrand~~ Factor, wherein the at least one single domain antibody corresponds to a sequence represented by SEQ ID NO: 5, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear ($1600\ s^{-1}$) condition at 1 μg/ml or at lower concentrations.

41. (Withdrawn and currently amended) A polypeptide or polypeptide construct comprising at least one single domain antibody directed against von Willebrand ~~Wilebrand~~ Factor, wherein the at least one single domain antibody corresponds to a sequence represented by SEQ ID NO: 7, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear ($1600\ s^{-1}$) condition at 1 μg/ml or at lower concentrations.

42. (Previously presented) A polypeptide or polypeptide construct comprising two or more single domain antibodies directed against von Willebrand Factor; and

wherein the two or more single domain antibodies correspond to a sequence represented by any of SEQ ID NO: 3, or to an homologous sequence of SEQ ID NO: 3 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at 1 μg/ml or at lower concentrations, or

wherein the two or more single domain antibodies correspond to a sequence represented by SEQ ID NO: 5, or to an homologous sequence of SEQ ID NO: 5 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at 1 μg/ml or at lower concentrations, or

wherein the two or more single domain antibodies correspond to a sequence represented by SEQ ID NO: 7, or to an homologous sequence of SEQ ID NO: 7 with a sequence identity of more than 70% with the parent sequence and wherein said homologous sequence is able to inhibit at least 50% of platelet aggregation under high shear (1600 s^{-1}) condition at 1 μg/ml or at lower concentrations.

43. (Previously presented) A polypeptide or polypeptide construct according to claim 1 in which at least one single domain antibody is a VHH domain.

44. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain comprising an amino acid at position 45 according to the Kabat numbering that is selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, proline, phenylalanine, tyrosine, tryptophan, methionine, serine, threonine, asparagine, and glutamine.

45. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain comprising an amino acid at position 103 according to the Kabat numbering selected from the group consisting of arginine, serine or an uncharged residue, optionally glycine.

46. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a VHH domain that is obtained by immunising a camel and obtaining hybridomas therefrom, or by cloning a library of single domain antibodies and subsequently selecting the VHH using phage display.

47. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is humanized.

48. (Previously presented) A polypeptide or polypeptide construct according to claim 1, in which at least one single domain antibody is a humanized VHH domain.

49. (Previously presented) A polypeptide or polypeptide construct according to claim 48, in which at least one single domain antibody is humanized by replacing one or more of the *Camelidae* amino acids by their human counterparts as found in a human consensus sequence.

50. (Previously presented) A polypeptide or polypeptide construct according to claim 48, in which at least one single domain antibody is humanized by replacing any of the following residues either alone or in combination: FR1 positions 1, 5, 28 and 30, the hallmark amino acids at FR2 positions 37, 44, 45 and 47, FR3 positions 74, 75, 76, 83, 84, 93 and 94 and FR4 positions 103, 104, 108 and 111, wherein the numbering of the positions is according to the Kabat numbering.

51. (Previously presented) A polypeptide or polypeptide construct according to claim 42 that comprises one or more single domain antibodies directed against the A1 domain of vWF.

52. (Previously presented) A polypeptide or polypeptide construct according to claim 42, in which the two or more single domain antibodies are of the same sequence.

53. (Previously presented) A polypeptide or polypeptide construct according to claim 42, in which the C-terminal end of the first single domain antibody is linked to the N-terminal end of the next single domain antibody.

54. (Previously presented) A polypeptide or polypeptide construct according to claim 42, wherein said polypeptide or polypeptide construct is not able to inhibit 50% or more of platelet aggregation under low shear (300 s^{-1}) condition at 10 μg/ml or at lower concentrations.

55. (Previously presented) A composition comprising a polypeptide or polypeptide construct according to claim 22, wherein the composition is formulated for oral, parenteral, intra-nasal, inhalation, intravenous, intramuscular, topical or subcutaneous administration.

56. (Previously presented) The polypeptide or polypeptide construct of claim 1, wherein the polypeptide or polypeptide is pegylated.

57. (Previously presented) The polypeptide or polypeptide construct of claim 2, wherein the polypeptide or polypeptide is pegylated.

58. (Previously presented) A composition comprising the pegylated polypeptide or polypeptide construct according to claim 56 and a pharmaceutically acceptable vehicle.

59. (Previously presented) A composition comprising the pegylated polypeptide or polypeptide construct according to claim 57 and a pharmaceutically acceptable vehicle.